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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,505	04/22/2004	Shan X. Wang	STAN-571 (S00-163)	6970

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,505	WANG ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 19-48* is/are pending in the application.

4a) Of the above claim(s) *20-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 19* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☒ Claim(s) *1-17, 19-48* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Priority

This application 10829505, with PG Pub. No. 20050100930 filed 04/22/2004, claims Priority from Provisional Application 60519378, filed 11/12/2003.

Child Data: Application 11655561, filed on 01/18/2007, now abandoned is a continuation in part of 10829505 , filed on 04/22/2004. Application 11804583, filed on 05/17/2007 is a division of 10829505 , filed on 04/22/2004.

Application 11938187, filed on 11/09/2007 is a division of 10829505 , filed on 04/22/2004

Amendment Entry & Claims Status

The amendment filed on October 5, 2009 has been acknowledged and entered.

Claims 1-17, 19 and newly added claim 48 are being examined.

Claims 20-47 are withdrawn.

Claimed Invention

1. (Currently Amended) A method of detecting a complex, the method comprising:

providing a first molecule bonded to at least one magnetizable nanoparticle;

providing a second molecule bonded to a substrate;

contacting the first molecule to the second molecule under conditions suitable for selective binding of the first molecule to the second molecule to form a complex; and

detecting the complex, wherein said detecting comprises applying a DC bias field and an AC tickling field.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10, 11, 17, 19 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox (WO 01/14591, published March 1, 2001) in view of Dames (US 6,323,770).

Fox teaches a method of detecting a molecule of interest, the method comprises providing a first molecule bonded to a magnetizable nanoparticle; providing a second molecule bonded to a substrate; contacting the first molecule with the second molecule to promote binding between the two molecules to form a complex; detecting the complex. (see pg. 20, lines 15-18; pg. 6, lines 15-20). For claims 2-8, Fox teaches that the target molecule/specific binding molecule (first molecule or second molecule respectively) are among proteins (antigens/antibodies), polypeptides, nucleic acids (see pg. 11, lines 14-15; pg. 20, lines 14-15; pg. 21, lines 6-7). For claims 10-11, Fox teaches that the magnetic particles are ferromagnetic, ferrimagnetic, paramagnetic or superparamagnetic. (see pg. 8, lines 20-23). Fox teaches using a sensitive giant

magnetoresistive ratio sensor (GMR) to detect the complex. The GMR sensor advantageously includes biasing magnets for producing an applied biasing magnetic field. The input voltage and the output sensor are routed to an operational amplifier and the output signal (net signal) is measured. This output signal will vary with the intensity of the an externally applied magnetic field. (for claims 17 and 19). (see pg. 13, line 25-pg. 14, line 10).

However, Fox fails to teach that said detecting comprises applying a DC bias field and an AC tickling field.

Dames teaches using a DC current and AC current to detect a magnetic tag. The DC current is applied to the magnetic tag and an AC current is then applied. This AC current is caused to flow in opposite direction of the DC current. (see col. 5, lines 40-51; col. 6, lines 37-65).

It would have been obvious to one of ordinary skills in the art to apply the concept of using DC current and AC current (low frequency AC tickling field) to detect magnetic response of a magnetic tag as taught by Dames to the method of Fox to detect predetermined region of a magnetic marker or particles in assay.

Claims 1-8, 10, 11, 14-17, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coehoorn et al. (WO 03/054523, published July 3, 2003) in view of Dames (US 6,323,770).

Coehoorn teaches a method of magnetic detection comprising providing biological molecules on a substrate of a magnetoresistive device; adding magnetic nanoparticles conjugated with binding molecules specific for the biological molecules on the substrate of the magnetoresistive device so that the biological molecules on the substrate and the nanoparticles form a complex; detecting such complex. (see abstract; pg. 5, lines 18-30). For claims 2-8, Coehoorn teaches the molecules are DNA, RNA, proteins (antigens or antibodies), or peptides, etc. (see pg. 8, lines 3-20). For claims 10 and 11, Coehoorn teaches that the magnetic nanoparticles are superparamagnetic . For claims 14 and 15, Coehoorn teaches that the magnetic nanoparticles diameter range between and 250 nm, preferably between 3 and 100 nm, or 10 and 60 nm. (see pg. 5, lines 28-36). For claim 16, Coehoorn teaches using a spin-valve substrate. (see table on pg. 23). For claims 17 and 19, Coehoorn teaches an external magnetic field is applied and a net signal generated by the magnetic field in the plane of the GMR elements is detected. (see pg. 11, lines 17-19; pg. 11, lines 28-33).

However, Coehoorn fails to teach said detecting comprises applying a DC bias field and an AC tickling field.

Dames teaches using a DC current and AC current to detect a magnetic tag. The DC current is applied to the magnetic tag and an AC current is then applied. This AC current is caused to flow in opposite direction of the DC current. (see col. 5, lines 40-51; col. 6, lines 37-65).

It would have been obvious to one of ordinary skills in the art to apply the concept of using DC current and AC current (low frequency AC tickling field) to detect

magnetic response of a magnetic tag as taught by Dames to the method of Coehoorn to detect predetermined region of a magnetic marker or particles in assay.

Claims 1, 2-8, 10, 11, 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselt (US 5,981,297, Nov. 9, 1999) in view of Dames (US 6,323,770).

Baselt teaches a method for detecting target molecules. The method comprises providing a recognition molecules bound to a surface of a magnetic field sensor; adding target molecules bound to magnetic particles; exposing the magnetic particles bound target molecules to the surface of the magnetic field sensor bound recognition molecules so that the molecules form a complex; detecting such complex. (see col. 3, lines 39-59). For claims 2-8, Baselt teaches that the recognition molecules or the target molecules are peptides, antibodies, DNA or RNA, proteins, etc. (see col. 4, lines 3-7). For claims 10 and 11, Baselt teaches that the magnetic particles are superparamagnetic (see col. 3, lines 60-65). For claim 17, Baselt teaches applying an external magnetic field to detect the complex. (see col. 7, lines 25-30). For claim 19, Baselt teaches detecting a net signal or resistance change in the magnetoresistive element. (see col. 8, lines 8-24).

However, Baselt fails to teach said detecting comprises applying a DC bias field and an AC tickling field.

Dames teaches using a DC current and AC current to detect a magnetic tag. The DC current is applied to the magnetic tag and an AC current is then applied. This AC current is caused to flow in opposite direction of the DC current. (see col. 5, lines 40-51; col. 6, lines 37-65).

It would have been obvious to one of ordinary skills in the art to apply the concept of using DC current and AC current (low frequency AC tickling field) to detect magnetic response of a magnetic tag as taught by Dames to the method of Baselt to detect predetermined region of a magnetic marker or particles in assay.

Claims 1-8, 10, 11, 14, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terstappen et al. (US 6,623,983, September 23, 2003) in view of Dames (US 6,323,770).

Terstappen teaches a method for immobilizing magnetically labeled particulate entities on a collection surface via binding between specific binding pair members. The method comprises providing one member of a specific binding pair bound to the collection surface and the other member bound to magnetic nanoparticles; exposing the magnetic nanoparticles bound binding member to the collection surface to form a complex between the binding members; detecting said complex. (see col. 6, lines 18-50;col. 12, lines 53-57). For claims 2-8, Terstappen teaches the binding members are proteins (antibodies, antigens, peptides,) or RNA or DNA. (see col. 8, lines 50-55; col. 9, lines 20-25; col. 10, lines 29-30). For claims 10 and 11, Terstappen teaches that the magnetic nanoparticles are superparamagnetic. (see col. 2, lines 42-44). For claims 14

and 15, Terstappen teaches the diameter of the magnetic nanoparticles range from 20-25 nm (see col. 2, line 53) or less than 200 nm. (see col. 9,line 64).

However, Terstappen fails to teach said detecting comprises applying a DC bias field and an AC tickling field.

Dames teaches using a DC current and AC current to detect a magnetic tag. The DC current is applied to the magnetic tag and an AC current is then applied. This AC current is caused to flow in opposite direction of the DC current. (see col. 5, lines 40-51; col. 6, lines 37-65).

It would have been obvious to one of ordinary skills in the art to apply the concept of using DC current and AC current (low frequency AC tickling field) to detect magnetic response of a magnetic tag as taught by Dames to the method of Terstappen to detect predetermined region of a magnetic marker or particles in assay.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox, or Baselt or Coehoorn in view of Dames as applied to claim 1, and further in view of Berning et al. (PGPub US 2005/0025969).

Fox, Baselt, Coehoorn and Dames have been discussed above.

However, they fail to teach that the first molecule is covalently bonded to at least one magnetizable nanoparticle by a gold-thiol linkage, and the nanoparticle comprises a noble metal surface layer such as a gold surface layer.

Berning teaches nanoparticles coated with a layer of gold including a magnetic nanoparticle central core, and a coating of gold completely encapsulating the magnetic nanoparticle central core. The composite further comprises thiol-bound functional group-containing spacer groups thereon the gold-coated magnetic nanoparticles. (see [0009]. The gold-coated magnetic nanoparticles are further coupled to recognition group such as proteins, peptides, nucleic acids, (see [0014]. The size of the magnetic nanoparticles range from 10 nm to 250 nm. (see [0011]).

It would have been obvious to one of ordinary skills in the art to use the magnetic nanoparticles coated with a gold surface layer and thiol group as taught by Berning the method of Fox, Baselt or Coehoorn because such gold-coated magnetic nanoparticles of Berning would prevent direct bio-contact to the magnetic material thus improving biocompatibility. A gold surface also allows good coupling through chemical attachment of binding agents or recognition agents such as peptides, proteins or nucleic acids. (see Berning [0010]).

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fox or Baselt in view of Ferreira et al. (Journal of Applied Physics Vol. 93, No. 10, 15 May 2003, pp. 7281-7286 submitted by Applicants).

Fox and Baselt have been discussed above.

However, they fail to teach the substrate comprises a high sensitivity spin valve or a magnetic tunnel junction detector array.

Ferreira teaches using arrays spin valve sensors to detect magnetically labeled biomolecules. (See abstract, pg. 7282, col. 1, A).

Since Fox and Baselt teaches using GMR elements, it would have been obvious to one of ordinary skills in the art to use the spin valve element of GMR as taught by Ferreira to detect magnetic beads since spin valve-type GMR is a highly sensitive magnetic sensor element which exhibits a high-signal to noise ratio of output and stable operation.

Allowable Subject Matter

Claim 48 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior arts fail to teach that the AC field is applied orthogonally to the DC field.

Dames teaches applying AC current opposite to the DC current but not orthogonally.

Response to Arguments

Applicant's arguments with respect to claims 1-17 and 19 have been considered but are moot in view of the new ground(s) of rejection.

With regards to all of the 103 rejections, Applicants argue that one of ordinary skill in the art would have no objective reason to combine the secondary reference of

Dames to any of the primary references in all the 103 rejections because Dames teaches using DC current and AC current for interrogating macroscale magnetic tags, not "magnetic nanoparticles" as claimed.

This is not found persuasive because the secondary reference is relied upon for the teaching of a method of measuring the magnetic signal from a magnetic tag and nanoparticles in the primary references are magnetic tags or markers (regardless of their dimensions). Dames is not relied upon for the teaching of the size of the magnetic nanoparticles as claimed in the present invention. One of ordinary skills in the art would have a reason to combine the primary references with Dames because the primary references teaches detecting a net signal and Dames teaches applying a DC current to create a zero or field or magnetic null and applying an AC field which is an interrogating field and interacts with the magnetic tag to create a detectable response which is also a net signal. This AC field or interrogating field allows very small regions of the magnetic marker to be interrogated or detected. Furthermore, one of ordinary skills in the art would have a reason to combine Dames with the primary references because Dames and the primary references teach detecting magnetic materials (regardless of their dimension).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641